Model based analysis of cerebrovascular oscillation using the system Circle of Willis

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Abstract—Low frequency fluctuation (oscillation) can be observed in the cerebral blood flow under the following condition. The physiological phenomenon’s frequency range is about 3–20 cpm (0.05 – 0.3 Hz). Independent from location, in both of the hemispheres the observed phenomenon shows high level of correlation, although previously its local enhancement was proved. The concrete physiological mechanism, controlling this oscillation has not been identified. One potential natural reason for the synchronous appearance of the oscillation is the structure of arteries, on the base of the brain, the so called Circle of Willis (CoW). In order to analyze the potential causes, physiological phenomenon’s controlling mechanism, the CoW model has been modified in order to reflect the experimental setup. In this paper we demonstrate the evaluation of the measurement, the modified model and present the simulation results.

I. INTRODUCTION

A low frequency flow fluctuation (oscillation) can be observed in the cerebral microcirculation of mice. It caused by the inhibition of a substance L-Name. The L-Name occurs acute NO-deficiency, that leads to hypersensitivity to thromboxane receptor mediated cerebral blood flow (hereunder CBF) oscillations [1]. During the experiments the microvascular CBF of tissues were observed in-vivo by a relative new measurement technology, called Lasca (Laser Speckle Contrast Analysis) [2].

A. Physiological phenomenon

The observed phenomenon, introduced above was identified as so-called Vasomotion by Physiologists [1]. Vasomotion is the oscillation of vascular tone or vascular diameter. During vasomotion, vessel segments of variable lengths contract rhythmically with frequencies of typically 3–20 cpm (0.05 – 0.3 Hz). It can be found in several frequency ranges, typically for a low-frequency domain, but it was reported also about higher frequencies [3]. During the measurement in our case the observed fluctuation’s frequency range amounts about 3 – 12 cpm; 0.06 – 0.2 Hz.) Vasomotion is typical for numerous muscular vessels [4]. This phenomenon conduction not purposive the adaptation of perfusion. It’s about the rhythmic alternations of contraction-state of smooth muscle fibers in the region of arterioles, metarterioles and pre-capillary sphincters. The effects occur independent from innervation [5].

In our case the physiological background of the phenomenon is not clarified in details. Several causes were excluded (breath, heart beat) experimentally, but the physiological processes controlling its appearance have not been identified. The potential mechanisms are: local flow regulation (autoregulation mechanisms), the most likely occasion is neuronal mechanism. Furthermore, the oscillations in the two hemispheres were highly synchronized independent from the location of the measurement. A previously work [1] presented about a local enhancement of the phenomenon, so it has to be a mechanism, which is able to execute the synchronization between the independent hemispheres. This work appoints to clarify the occasion for the propagation of the considered low-frequency oscillation developed in one hemisphere (or in its local region) to the other hemisphere (or to another region) with high level of synchronization.

Our hypothesis is that a mechanism controls the synchronization on the arbitrary “decoupled” regions. On the one hand, this mechanism can be a directly controller with neural source, on the other hand a not directly mechanism, that aims to regulate another physiological phenomenon, however it should make the hemispheres synchronized. The circle of willis is a ringlike vessel system at the basiranium, which may serve as a propagator of this fluctuation. The goal of this paper is to analyse a possibly effect of this system [6], with the extension for the metabolic autoregulation [7]. The simulation also allows saving efforts on animal researches, and to exclude or prove mathematically the transmitting role of the considered mechanism on the observed physiological phenomenon.

II. METHODS

A. Correlation analysis

By analyzing the spatial extension of the considered phenomenon, numerous conclusions can be drawn about its feature. A simple and reliable method is the crosscorrelation analysis. The cross-correlation analysis gives an information of the linear correspondence of two sequences (1). The degree of correlation was measured between time series from various locations of the brain tissue. The calculations were executed in Matlab. Firstly to generate zero-mean times series, the DC
A mathematical model suggested by Moorhead et al. [9][6] describes the Circle of Willis (CoW), and the function of metabolic autoregulation regarding to the arterioles, capillaries between the efferent arteries, coming out of CoW and the venous vessels. The presented microcirculation system (arterioles, capillaries) is modeled as vessels ($ACA_2$, $MCA$, $RCA$ see Fig. 3). The CoW is a ringlike structure of arteries so-called anastomosis, see Fig.3, which is placed beneath the hypothalamus at the basi-craniun. This structure collects and shares the oxygen rich blood, coming from the heart, to the cerebral tissues. It can be modeled as one-dimensional system. As the blood flow in the CoW can be handled as laminar flow, the blood as newtonian fluid; viscous and incompressible, and the vessels as axis-symmetric, it follows that the Poiseuille Equation (2) and the equations for the conservation of mass (4) can be used for determine the condition of flow rate in the arteries and the pressure at the junction of arteries in the CoW [9][6]. The Poiseuille Equation creates a relationship between the pressure drop and the flow rate, as the equations of conservation of mass, defines that the flow rate in the input arteries of a junction is equal to the flow rate in the output arteries. The above introduced equations are described as follows:

$$q = \frac{\Delta P}{R}$$  \hspace{1cm} (2)

$$R = \frac{8\mu d}{\pi r^4}$$  \hspace{1cm} (3)
\[ \sum q = 0 \] (4)

where \( q \) is the flow rate of blood, \( R \) is the resistance of arteries. \( \Delta P \) defines the pressure differences between artery-junctions in the CoW. The \( r \) is the radius of arteries and \( \mu \) is the viscosity of the blood.

Based on the functionality, the system’s arteries are classified in three groups. These are the afferent-, circulus- and efferent arteries [9]. There are three afferent arteries; Basilar Artery (BA), Left- and Right Internal Carotid Arteries (LICA, RICA) and six efferent arteries; Left- and Right Anterior Cerebral Artery 2 Segment (LACA2, RACA2), Left- and Right Middle Cerebral Artery (LMCA, RMCA), Left- and Right Posterior Cerebral Artery 2 Segment (LPCA2, RPCA2).

Each vessel is characterized by its resistance, which can be described as the inverse proportional to the vessel radius (3). The pressure rate at the vessel junctions and flow rate in arteries can be affected by varying the resistances, so the radius of the vessels.

The efferent arteries are characterized by the varying resistances, modeling the autoregulation mechanism of the cerebral micro circular system components, as arterioles, capillaries. It follows that the parameters of these system are found in other order of magnitude, than the parameter (resistance) of circulus- and afferent arteries.

The metabolic autoregulation mechanism tries to keep the flow rate in the efferent arteries constant, to ensure the oxygenation level of tissues continuously [6]. The system is driven by the flow rate in the efferent arteries. If the flow rate in the efferent arteries changes, in case of dysfunction of afferent- or circulus arteries, the mechanism acts by changing their resistance. If the resistance changes, the flow rate also changes. The model represents the dynamics of the autoregulation mechanism in two steps by PID controller [7]. The equation describing the system behavior can be summerized in a matrix equation (5):

\[ Ax = b \] (5)

where \( A \) contains the resistance, \( x \) sums up the system variables, like the flow rate in the vessels and the pressure value at the vessel nodes. The vector \( b \) comprises the input- and output pressures as the boundary conditions of the system.

### D. Role of the model on the transmitting of the phenomenon

We assume, that the phenomenon vasomotion, enhanced in an arbitrary location of the one hemisphere by the acute NO-deficiency, can be observed on the efferent arteries of the CoW in some degree. According to the measurements, it is theoretical possible. As the blood circulation of both hemispheres is only connected through CoW directly, the fluctuation can be extended physically to the other side of the brain through this system, also acting the metabolic autoregulation mechanism, which tries to keep the oxygenation of the tissues constant and smooth.

The physiological parameters for the simulations, obtained from the work of Moorhead et al. [6] kept unchange. Summarized, the method contains the following steps:

1) It is assumed that the low frequency fluctuation is (scenario specific) superponated on flow rate of microcirculation system modeled by one efferent vessel, as the vasomotion is independent from the metabolic autoregulation mechanism. This means, that the system

### TABLE I

<table>
<thead>
<tr>
<th>Scenario nr.</th>
<th>Driven vessels</th>
<th>Additive noise</th>
<th>Heartbeat</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>LPCA2, LMCA, LACA2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>LMCA</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>LPCA2, LMCA</td>
<td>x</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>LMCA</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>

### E. Modified computational model

According to previous section, CoW is assumed to be the transmitter of the phenomenon vasomotion.

In order to analyze our hypothesis, we modified the computational model. The modification implies the incorporation of the vasomotion phenomenon with the autoregulation mechanism through the flow rate. The fluctuation is superponated on the efferent arteries. The autoregulation control ability and the damping behavior of the CoW can be measured based on the modified mathematical model. It also gives the answer for the primary question, if the local enhanced vasomotion can be compensated by the metabolic autoregulation mechanism in the other hemisphere transmitted through the CoW.

Fig. 3. 1D flow model for the CoW and the autoregulation mechanism suggested by Moorhead et al. [6]. The system is symmetric and contains afferent- (BA, L/RICA) circulus- (L/RPCA1, L/RPCoA, L/RACA1 and ACoA) and efferent- (R/LPCA2, R/LMCA, and R/LACA2) arteries. The efferent arteries comprise the features of smaller arterioles and capillaries. The features are modeled as resistances. The resistances of efferent arteries are varying in function of the flow rate, through the metabolic autoregulation.
Fig. 4. The result of the simulation (scenario Nr.1) shows the relationship of flow rates between the RPCA2 and LPCA2 efferent arteries. The considered arteries are symmetric pairs of each other. By the reason of the resistances of arteries and the metabolic autoregulation mechanism the synchronous- and oscillation properties are not to see. The Fig. 5 shows this figure enlarged along the flow rates axis.

is excited from it’s outputs.

2) The fluctuation can be measured on the efferent arteries of CoW.

3) The fluctuation in flowrate of the efferent arteries activates the metabolic autoregulation mechanism by varying the radius so the resistance of vessels.

4) Resolve the system based on the updated resistances. It’s done by resolving the system of linear equations, see Eq. (5).

5) The varied resistances are to eliminate the fluctuation and, in addition they cause a slightly improved flowrate in the other vessels of the CoW (circulus arteries).

6) the rate of the propagation (amplitude magnitude, phase relationship) is analyzed.

Several simulatin conditions were analyzed according to efferent vessels, on which the fluctuation could be measured. These conditions are listed in details on Table I.

III. RESULTS AND DISCUSSION

The results of the simulation (see Fig. 4 to Fig. 9) show markedly, that the considered flow rates, grown up in the efferent arteries scenario specific, and on the opposite side of the hemispheres and also in the other arteries, are proved to be unsynchronized and the signals’ amplitude are found in different order of magnitude too. The difference is significant. In sum the mechanism CoW itself is not able to cause the synchronous appearance of the considered physiological phenomenon. The mechanism could play a role as propagator by the considered phenomenon, but only in connection with other physiological mechanism.

IV. CONCLUSION

It is proved that CoW alone is not able to be the occasion for propagation of vasomotion from one hemisphere to the other.

Fig. 5. The Fig. 4 was enlarged along the flow rate axis. It shows that the oscillation was propagated, but its amplitude was damped appreciably (other order of magnitude), and the sequences are also out-of-phase.

Fig. 6. The relationship among the flowrate of LMCA and RMCA arteries by the simulation (scenario Nr.1) shows the same results as on the Fig. 4.

So the hypothesis that the oscillation signal of frequency range of vasomotion is transmitted though the CoW extended by the metabolic autoregulation is false. Even so the simulation excludes the CoW as a possible mechanism in the research of determining the source and the control of the observed physiological phenomenon, vasomotion, saving effort on numerous animal experimentations and so a plenty of time.

V. FUTURE WORK

In the interest of improvement on the quality of the simulation, the oscillation phenomenon’s characteristic should be analyzed in detail. Other autoregulation processes have to be also taken into the investigation. In the next steps the sequences from the observation should be further analyzed in time- and frequency domain. On the other side the mechanism CoW can be extended or incorporated by further models of
Fig. 7. The result of the simulation (scenario Nr.2) shows the relationship of flow rates between the LMCA, RMCA and LPCA2 efferent arteries. The considered arteries are found on the contradictory sides. By the reason of the resistances of arteries and the metabolic autoregulation mechanism the synchronisation and oscillation characters are only slightly transmitted.

Fig. 8. The result of the simulation (scenario Nr.3) shows the relationship of flow rates between the LPCA2 and RMCA efferent arteries. The considered arteries are found on the contradictory sides. By the reason of the resistances of arteries and the metabolic autoregulation mechanism the synchronisation and oscillation characters are only slightly transmitted.

Fig. 9. The result of the simulation (scenario Nr.4) shows the relationship of flow rates between the LMCA and RMCA efferent arteries. On the afferent arteries were the effect of the heartbeat to see. The considered arteries are found on the contradictory sides. By the reason of the resistance of arteries and the metabolic autoregulation mechanism the synchronisation and oscillation characters are only slightly transmitted.

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Physiological phenomenon such as oxygenation process of cerebral tissues by capillary system.

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